

Limitations of Existing Endpoints for Premium IOLs

Malvina B. Eydelman, M.D.

Director

Division of Ophthalmic and Ear, Nose and Throat Devices



Disclosure

No Financial Relationships to Disclose



IDE Study Approval vs. Available Study Recommendations

Monofocal IOLS:

- » FDA recognized ANSI/ISO standards
 - Preclinical and clinical recommendations clearly delineated
- » 71% total IDEs (FY'05-FY'12) were approved or approved with conditions within first round

Premium IOLs:

- » Few recognized ANSI/ ISO Standards
 - Several endpoints not clearly delineated
- » 39% total IDEs (FY'05-FY'12) were approved or approved with conditions within first round



Aphakic Monofocal IOL Investigations (ISO 11979-7)¹

Effectiveness

» Best Corrected Visual Acuity (BCVA)

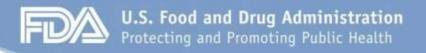
Safety

- » Safety and Performance Endpoints (SPE²) rates for Adverse Events (AEs)
 - corneal edema
 - hypopyon
 - intraocular infection
 - secondary surgical intervention
 - raised IOP requiring treatment
- » IOL tilt / Decentration

- cystoid macular edema
- pupillary block
- retinal detachment
- iritis

¹ FDA Recognized Standard

² Basic historical safety and effectiveness data (FDA Grid) incorporated in ISO 11979-7





Phakic Monofocal IOL investigations (ISO 11979-10, ANSI Z80.13)¹

Effectiveness – BCVA plus:

- Best Distance Corrected Near Visual Acuity
- Uncorrected Near Visual Acuity (ANSI only)
- Uncorrected Distance Acuity (UCDA)

Safety – SPE plus:

- Endothelial Cell Loss
- IOL Tilt / Decentration
- Contrast Sensitivity
- Crystalline lens status
- Clearance analysis (e.g., IOL-cornea)
- Subject Questionnaire
- AEs related to IOL design

¹ FDA Recognized Standards



Aphakic Multifocal IOL Investigations (ISO 11979-9 and ANSI Z80.12)¹

Effectiveness – BCVA² plus:

- Uncorrected Near VA, Uncorrected Distance VA²
- Distance Corrected Near VA (DCNVA)²
- Defocus curve (depth of focus)³

Safety – SPE plus:

- Explants for optical / visual reasons
- Mesopic DCNVA
- IOL Tilt / Decentration
- Contrast sensitivity⁴
- Fundus visualization
- Functional performance (night driving testing)⁴
- Subject Questionnaire (visual symptoms/aberrations)

¹ FDA Recognized Standards

², Monocular and Binocular; ³ Binocular; ⁴Outcomes compared to a concurrently run monofocal IOL control group.



Toric IOL Investigations: Aphakic and Phakic (ISO 11979-7 DIS and ANSI Z80.30)

- Effectiveness¹ BCVA plus:
 - » Evaluation of Cylinder
 - refractive cylinder, IOL misalignment, IOL rotational stability,
 pre-op and postop keratometry
 - » UCVA
- Safety SPE plus:
 - » IOL Tilt / Decentration
 - » Subject Questionnaire (visual symptoms/aberrations)²

¹ Effectiveness Outcomes are compared to those associated with a concurrently run non-toric IOL (similar design) control group for the lowest power only

² For ISO only, if necessary based on risk analysis



Aphakic Accommodative Investigations (ISO 11979-7 DIS and ANSI Z80.30 (Draft))

Effectiveness – BCVA plus:

- Distance, Intermediate, Near UCVA
- Intermediate and Near VA with Best Correction for Distance
- BCNVA and Add Power
- Accommodative Amplitude (AA) (objective testing, 1 D min.) / Assess AA Stability

Safety – SPE plus:

- IOL Tilt / Decentration
- Contrast Sensitivity
- Subject Questionnaire
- AEs related to IOL design



Limitations of Current Standards for Premium IOLs

Performance Criteria

- » SPE
 - Key safety outcome in all standards
 - Entry of premium IOLs to the marketplace highlight limitations (e.g., different rates of secondary surgical interventions)

Testing

- » Some recommended tests for "Premium" IOLs do not have well established methodologies
 - IOL tilt/decentration
 - Objective method for anterior subcapsular cataract and posterior capsular opacification
 - Accommodation
 - Functional performance (e.g. reading speed, night driving)
 - Patient Reported Outcomes



Introduction of Extended Depth of Focus (EDOF) IOLs

- New Category of IOLs for Improved Near and Intermediate Performance
- No current standards or draft standards
- No guidance
- Today the first public discussion of probable requirements for preclinical and clinical testing



Today's Focus on Areas with Highest Impact

- Premium IOL Safety Assessments
- Patient Reported Outcome (PRO) Measures
- Objective Assessments of Accommodation
- Subjective Assessments of Accommodation and EDOF



Premium IOL Safety Assessment

Concerns with historical adverse event (AE) rates currently used as safety benchmarks:

- May not reflect current standard cataract surgery instrumentation and techniques
- Different types of AEs with premium IOLs
- Acceptable rates of AEs with premium IOLs may be different
 - » Different risks/benefits for premium vs. monofocal IOLs



Patient-Reported Outcomes (PROs)

- Concerns with currently used questionnaires
 - » Have not undergone psychometric evaluation
 - » Have not been evaluated for validity in the intended population
 - » Have not robustly shown that the scores are meaningful
 - » Have not been developed and evaluated for some concepts of interest



Assessment of Accommodation

- Limitations of subjective assessments:
 - » Cannot distinguish true accommodation from pseudoaccommodation
 - » Affected by multiple non-specific factors → bias (overestimates)
- Objective assessments outstanding issues:
 - » Optical: Can they be used with all lenses?
 - » Biometric: difficulties with ocular fixation, stimulation of accommodation, and conversion to optical diopters
 - » Need standardization of procedures?
- ANSI/ISO standards call for objective measurements to minimize limitations of subjective assessments



Subjective Assessment of Accommodation and Extended Depth of Focus (EDOF)

- Concerns with subjective evaluations of accommodation and depth of focus
 - » Current subjective methods
 - may not be adequate to differentiate true performance difference from placebo effect (e.g., effects of patient squinting, blur interpretation)
 - may not accurately assess accommodation
- In EDOF subjects manifest refractions may have high variability
- No current standards or guidance exist to assist in the development of EDOF IOLs



Development of Endpoints for Premium IOLS

The Fastest Route To Market

